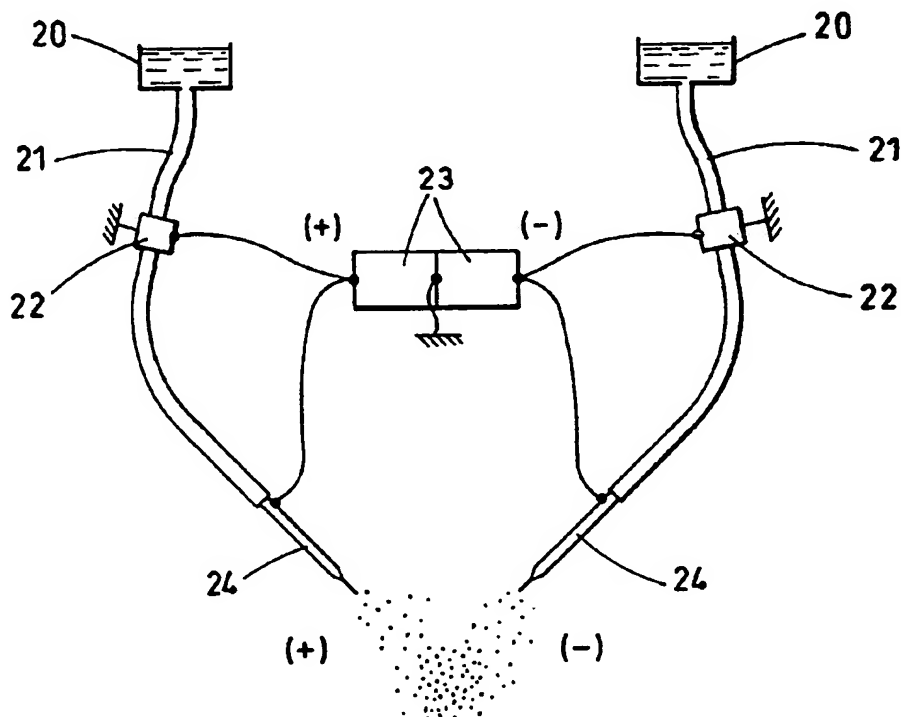




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(54) Title: DISPENSING DEVICE



(57) Abstract

A device for comminuting a liquid, which comprises at least two electrohydrodynamic comminution means (24) arranged so that in use comminution of opposing polarity are formed which are substantially admixed after formation and a pump (22) for use in the dispensing device.

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DISPENSING DEVICE

The invention relates to a dispensing device for comminuting a liquid, means
5 for supplying liquid for use in such device and the use of such a device, in particular,
in medicine.

Dispensing devices are known which produce a finely divided spray of liquid
droplets by electrostatic means (more properly referred to as 'electrohydrodynamic'
means). Electrohydrodynamic sprayers have found use in many areas of industry,
10 especially in agriculture for crop spraying, paint spraying in the automotive industry
and also in medicine for the administration of medicaments by inhalation.

The droplet spray in such devices is generated by applying an electric field to
a liquid located at a spray head or spray edge. The potential of the electric field is
sufficiently high to provide comminution of electrically charged liquid droplets from
15 the spray head. The electrical charge on the droplets prevents them from coagulating
via mutual repulsion.

United Kingdom patent number 1569707 describes an electrohydrodynamic
spray device principally for use in crop spraying. An stated essential component of
the GB 1569707 spray device is a field intensifying electrode, cited adjacent the spray
20 head and maintained at the same potential as the spray head. The field intensifying
electrode is not supplied with liquid. In use it is stated to reduce the incidence of
corona discharge which interfere with spray production and thereby allows lower
electric field strengths to be used during spray generation.

United States patent number 4703891 describes an crop spraying apparatus for
25 spraying liquids from a vehicle such as an aircraft or other airborne vehicle, having at
least two sprayheads arranged to produce spray of positive charge at one sprayhead
and negative charge at the other. The resulting charged sprays are then applied to the
relevant crops.

In many circumstances it is desirable to partially or wholly remove the electric
30 charge from droplet sprays produced by electrohydrodynamic comminution devices
in a controlled manner. To date the principal method used to effect comminution
discharge has required the use of a discharging electrode having a sharp or pointed
edge and located downstream from the spray head. The discharging electrode
produces a cloud of charged ions from the surrounding air having an opposite
35 electrical charge of equal magnitude to that on the comminuted liquid spray. In use,
the ion cloud is attracted towards, collides with and thereby neutralizes the liquid
spray.

United Kingdom patent number 2018627B discloses an electrohydrodynamic
spray device wherein the electric charge on the droplet spray is fully or partially

removed by means of a discharge electrode. The UK 2018627B device is stated to provide discharged or partially discharged sprays for crop spraying purposes. European Patent number 0234842 discloses an electrohydrodynamic inhaler wherein the spray of charged droplets is similarly discharged by means of a discharge
5 electrode. The droplets are discharged in order to facilitate droplet deposition into the respiratory tract as otherwise the electrically charged droplets would deposit onto the mouth and throat of the user.

A particular problem associated with the use of the sharp discharge electrode is that the highly mobile ion cloud from the discharge electrode often interferes with
10 the comminution of the liquid spray. The inhaler device of EP 0234842 attempts to ameliorate the effects of the ion cloud at the spray head by using a neutral shield electrode located close to the spray head.

It is a primary feature of the present invention that a device for comminuting a liquid is provided, which comminutes the liquid by electrohydrodynamic means and
15 which produces a partially or fully electrically discharged comminution without the need for the sharp discharge electrode described above. The present device does not have the problems associated with the discharge electrode and hence it does not require the use of a neutral shield electrode.

Accordingly, there is provided a device for comminuting a liquid, which
20 comprises at least two electrohydrodynamic comminution means arranged so that in use comminutions of opposing polarity are formed which are substantially admixed after formation.

The electrohydrodynamic comminution means may be any conventional electrohydrodynamic comminution means, for example those described in the above
25 mentioned patent specifications.

Suitably, each comminution means comprises a comminution site, generally being a surface or edge, from which the liquid comminution is produced.

A preferred comminution surface or edge is provided by a thin capillary tube, a nozzle or a slot defined by two parallel plates. However any comminution surface
30 or edge described in the above mentioned patent specifications may be used.

The device generally comprises an even number of comminution means but this is not essential, the key factors are that at least two of the comminution means provide comminutions of opposing polarity and that the comminutions produced are arranged to substantially admix.

Suitably, the device comprises 2, 4 or 6 comminution means, however higher
35 numbers can be used as required. An example of a device is that which has 2 comminution means. An example of a device is that which has 6 comminution means.

Suitably, each comminution means comprises a means for supplying liquid to the comminution site.

Appropriate means for supplying liquid to the comminution site include mechanical, electrical or electronic powered means such as pumps which are capable
5 of providing the required flow rate of liquid to the comminution site.

The comminution means of the invention can be used with a large range of flow rates, but generally operates with flow rates in the range of between 0.1 to 500 μ L per second, such as 0.5 to 5 μ L per second, especially for inhaled administration, or 10 to 200 μ L per second, especially for agricultural use.

10 A suitable means for supplying the liquid includes a syringe pump or an electrically powered pump as described in EP 0029301.

It will be appreciated from the foregoing that the comminution means generally comprises a comminution site, a means for supplying a liquid to the comminution site and a means for electrically charging the comminution site to an
15 electric potential sufficient to comminute the liquid in use.

Accordingly, in one particular aspect of the invention there is provided a device for comminuting a liquid, which comprises at least two electrohydrodynamic comminution means each comprising a comminution site, a means for supplying a liquid to the comminution site and a means for electrically charging the comminution
20 site to an electric potential sufficient to comminute the liquid in use, wherein the comminution means are arranged so that in use comminutions of opposing polarity are formed which are then substantially admixed.

Suitably, each comminution means comprises a means for electrically charging the said comminution site to a potential sufficient to provide comminution
25 of the liquid, the potential usually being of the order of 1-20 kilovolts.

The means for electrically charging the said comminution site, such as a surface or edge, may be provided by any conventional high voltage generator having the appropriate output, one particularly convenient generator being a piezoelectric generator.

30 The piezoelectric material for the generator may be chosen from several types, such as barium titanate ceramic, or pvdf polymers, which generate significant high-voltage electric charge displacement upon being pressurized. The choice and capacity may be so chosen as to offer control of the degree of pumping and/or atomization when operated.

35 The required voltage for use is provided when the piezo-electric generators are squeezed, and again (with opposite polarity) when the piezo-electric generators are released from pressure.

The arrangement by which the comminutions are admixed enables the net charge on the admixed comminution to be either essentially neutral, positive or

negative. Generally, the residual positive or negative charges are less than the positive or negative charge on any of the premixed comminutions.

The net residual charge on the admixed comminution may be fixed for any given device or the arrangement may be such that the net residual charge on the admixed comminution may be regulated in a controlled manner. Thus the device of the invention optionally comprises a means for regulating the electrical charge on a comminution produced from any of the comminution means prior to admixture.

Suitable means for regulating the electrical charge on a comminution may be provided by a variety of methods, such as by incorporating a means for regulating the charging means so as to provide variable voltage output and/or a means for regulating the means for supplying a liquid to the comminution site so as to vary the liquid flow rate to the comminution site.

Suitable arrangements of the comminution means which enable the comminutions produced to be admixed includes any arrangement wherein the comminution means are relatively located so as to enable the comminutions to substantially admix. Favourably, the comminution means are arranged so that the comminutions produced are directed to converge into a mixing zone. For example, when the device comprises two comminution means they may be angled towards each other so as produce comminutions which converge into the mixing zone. Or when the device comprises three or more comminution means, they may be arranged so that the comminutions are directed to converge radially into the mixing zone. Alternatively, the relative location of the comminution means may be arranged such that the mutual attraction of the comminutions produced is sufficient to allow substantial admixing, for example they may be in a mutually parallel manner.

It is envisaged that a liquid supply means may supply one or more of the comminution means of the invention.

Alternatively, a liquid supply means may supply only one comminution means.

From the foregoing it will be appreciated that it is an aspect of the present invention that comminuted sprays from different liquids may be mixed as required. Such liquids may be capable of providing a new product on admixture or they may comprise components which are so capable. The device may also be used to mix two liquids which are reactive components of a rapid chemical reaction. In each case the mixed droplets may then be applied as a spray, with a charge-to-mass ratio on the droplets that will be the residual after the two opposing charges have been used to coalesce the liquids.

Similarly, the present device may be used to mix components which are incompatible one with the other and which therefore are advantageously admixed at the point of use.

Suitable liquids include liquids comprising components useful for human or animal health care, such as medicaments for pharmaceutical or public health care use or medically useful compounds such as anesthetics.

5 Suitable liquids include liquids comprising components for agricultural use such as pesticides or biocides.

 Suitable liquids include liquid cosmetic formulations.

 Other suitable liquids include paints and inks. Also included are liquids for providing aromas.

 Preferred liquids are pharmaceutically active liquids.

10 The comminution means of the dispenser provides liquid droplets within the range of from about 0.1 to about 500 microns in diameter: More usually from 0.1 to 200 microns, such as 1.0 to 200 microns: Examples include droplets within the range of 5.0 to 100, 0.1 to 25, 0.5 to 10 or 10 to 20 microns. A favoured range for inhaled administration is 0.1 to 25 or 0.5 to 10 microns, especially for administration to the
15 lower respiratory tract, and 10 to 25 microns, especially for administration to the upper respiratory tract.

 For a given liquid the diameter of the droplets can be controlled by varying the applied voltage and liquid flow rate using routine experimental procedures.

20 Liquids having viscosities within the range of from 1 to 500 centipoise and resistivities in the range of from 10^2 - 10^8 ohm m can be comminuted by the present device.

 One favoured use of the device of the invention is for the dispensation of a comminuted liquid for inhalation.

25 Accordingly, in one preferred aspect of the invention there is provided a device for comminuting a liquid for inhalation, which comprises at least two electrohydrodynamic comminution means each comprising a comminution site, a means for supplying a liquid to the comminution site and a means for charging the comminution site to an electric potential sufficient to comminute the liquid in use, wherein the comminution means are arranged so that in use comminutions of
30 opposing polarity are formed which are substantially admixed after formation.

 The device of the invention may be adapted into any embodiment form which dispenses comminuted liquid for inhalation, for both medicinal and non-medicinal use.

 Non-medicinal inhalation uses includes dispensing perfumes and aromas.

35 Preferably, the device is in the form of an inhaler, for the inhaled delivery of a medicament.

 A preferred liquid is therefore a liquid medicament formulation adapted for inhaled administration.

Medicaments suitable for adaption for inhaled administration include those used for the treatment of disorders of the respiratory tract, such as reversible airways obstruction and asthma and those used in the treatment and/or prophylaxis of disorders associated with pulmonary hypertension and of disorders associated with right heart failure by inhaled delivery.

Since the charge-to-mass ratio of an electrohydrodynamic comminution may sometimes require optimization, to a value that may lie anywhere between the unadjusted value at the moment of comminution, and zero, the device of the invention may also be used to optimize droplet charges. For example, in order to apply a liquid containing a therapeutic agent to specific airways within a human lung, by inhalation, it would be highly beneficial if the droplet mass and charge could be independently controlled. This would give an unprecedented degree of control over the zone of deposition of the droplets within the lung.

For example in a two nozzle dispensing device, it can be arranged to have one nozzle comminuting a spray of the medicament, such as a beta-2 agonist, for example salbutamol, where the average droplet charge $\pm Q_a$ could then be accurately adjusted by arranging for deionized water to be comminuted from the second nozzle with an average charge $\pm Q_b$, thus the desired final value on the inhaled spray of could be Q_a plus or minus Q_b .

Similarly, for example, in charged droplet spraying of crops it is sometimes highly beneficial if the droplet charge can be adjusted independently of its mass, in order to achieve penetration into dense foliage.

As indicated above, various means have been used to deliver liquid to the comminution site prior to comminution generation. Most are mechanical in nature although European Patent number 0029301 discloses a spray device incorporating a pump wherein the hydrostatic pressure is generated by an electric potential between two electrodes immersed in the feeder stream of the liquid to be sprayed. It is a further aspect of the present invention that there is provided a novel electrically powered pump, suitable for pumping liquid to the comminution site of an electrohydrodynamic comminution device.

An important component of the dispensing devices described above is the means for supplying the liquid to the comminution site. Accordingly, in a further aspect of the present invention there is provided a pump, suitable for supplying liquid to the comminution site of a comminution means, which pump comprises an electrically insulating conduit for the liquid, the conduit enclosing an electrically insulating solid permeable to liquid, means for retaining the solid within the conduit and means for applying an electric field across the solid, so that in use, when the electric field is applied, liquid is induced to flow through the solid and hence along the conduit.

The dimensions of the conduit are not considered to be limiting to the successful operation of the invention, the essential feature being the presence of an electric field across the solid.

A suitable means for applying an electric field across the solid is provided by a pair of permeable electrodes, spaced apart along the conduit.

It is preferred if the solid substantially fills the conduit. A suitable conduit is a pipe, for example a cylindrical pipe.

Conveniently, the means for applying an electric field across the solid also acts as the retaining means for the solid in the conduit.

In one suitable form of the invention a pair of permeable electrodes are fixed apart along the conduit and the permeable solid substantially fills the space defined by the electrodes and the inner wall or walls of the conduit.

Preferably, the electrodes are flat plates shaped to retain the solid within the conduit, thus when the conduit is a pipe the electrodes are disc shaped.

The permeable electrodes are conveniently constructed from wire gauze or from electrically conducting titanium oxide.

Suitably, the liquid permeable solid is in powdered form. Suitable powdered forms include powdered ceramic, powdered silica, powdered plastic and clay.

Alternatively, the liquid permeable solid may be a fibrous solid, suitably a fibrous ceramic or polymer fibres.

In addition as an alternative to powdered or fibrous forms the electrically insulating solid may be any permeable form of ceramic, silica, plastic or clay.

The relationship between flow rate, dimensions of the conduit, applied voltage and the nature of permeable solid may helpfully be described by the equation shown in Scheme (I) which assumes that the permeable solid is formed by a bundle of parallel capillary fibres of radius 'r':

Scheme (I)

$$\text{Flow rate} = \frac{n \epsilon_r \epsilon_0 \xi \pi r^2 \cdot V}{\eta L} \quad \text{m/sec}$$

wherein:

n = number of capillaries of radius r ,

V = applied voltage;

L = distance between electrodes;

ξ = Zeta potential;

ϵ_r = relative permittivity;

ϵ_0 = permittivity of free space; and

η = viscosity of the liquid.

Although Scheme (I) is considered to be useful for describing the theoretical basis for the pump of the present invention, the invention is not considered to be limited by the relationship set out in Scheme (I).

5 In a preferred form, when used to supply a liquid formulation in the dispensing device of the invention, the pump comprises an electrically insulating tube, a pair of electrodes permeable to liquid and fixed apart along the tube and a powdered solid permeable to liquid, the solid substantially filling the space defined by the electrodes and the inner wall of the tube and means for applying an electric field
10 to the electrodes, so that in use, when the field is applied, liquid is induced to flow through the solid and hence along the tube.

The above described liquid supply means allows an even liquid flow at precise rates, using the same (electrical) energy source that is used to generate the droplets thus requiring no mechanical means of pressurizing the liquid. The entire unit may
15 thus be powered by very small battery-driven voltage sources, or even by a hand-operated piezoelectric device such as a stack of PVdF film or barium titanate ceramic. The device may thus be made pocket-sized.

The invention also extends to the conduit, retaining means and means for applying the electric field as described above for use with the solid as defined above.

20 When used herein 'a comminution' includes a liquid droplet spray.

When used herein 'medicament' includes proprietary medicines, pharmaceutical medicines and veterinary medicines.

When used herein, unless more specifically defined herein, 'inhaled administration' includes administration to and via the upper respiratory tract,
25 including the nasal mucosa, and the lower respiratory tract.

When used herein 'electrically insulating' relates to a level of electrical insulation sufficient to allow an electric field to be applied across the solid, wherein the field is sufficient to induce liquid flow; preferably it includes semi and fully insulating materials.

30 When used herein the terms 'liquid permeable' or 'permeable to liquid' as applied to, for example, the solid and electrodes relate to solid and electrodes which are intrinsically permeable to liquid or to solid or electrodes which can be rendered permeable by processes for example, in the case of the solid, granulation or powdering or, for the electrode, by forming into shapes which allow the passage of
35 liquid, such as mesh shapes.

The liquid medicinal formulations for use in the device of the invention may be formulated according to conventional procedures, such as those disclosed in the US Pharmacopoeia, the European Pharmacopoeia, 2nd Edition, Martindale The Extra

Pharmacopoeia, 29th Edition, Pharmaceutical Press and the Veterinary Pharmacopoeia.

The liquid cosmetic formulations for use in the device of the invention may be formulated according to conventional procedures, such as those disclosed in
5 Harry's Cosmeticology, 9th Edition, 1982, George Goodwin, London.

The invention may now be described, by way of example, with reference to the accompanying drawings:

Figures 1 to 4 illustrate examples of comminution sites of the device of the invention; Figure 5 is a plan view illustrating a multi-nozzle comminution site of the device of
10 the invention;

Figures 6 and 7 illustrate examples of the liquid supply means of the device of the invention;

Figure 8 is a schematic drawing illustrating an example of a charging means of the device of the invention;

15 Figures 9 and 10 are schematic drawings each illustrating an example of a device of the invention;

Comminution sites

Figure 1 shows a thin-walled capillary tube (1), which may be made of conducting or semiconducting material and which may be electrically connected to a
20 source of high-voltage direct-current, either directly or through the liquid. A single jet (3) is produced from a cusp (2) of liquid, both of which form naturally, according to the voltage and flow rate for a given liquid.

Fig. 2 shows a similar tube (1) used at a lower flow rate and voltage which are adjusted so as to produce multiple cusps (2) and jets (3) issuing from the region of the
25 ends of the thin-walled tube (1).

Fig. 3 shows a conducting or semiconducting cylinder (1) which may have a larger diameter than those shown in figs. 1 and 2. This nozzle has an inner-member, (4) which is approximately coaxial with the outer tube, (1).

Fig. 4 shows a slot nozzle, formed between two parallel plates (2) having
30 conducting, or semiconducting edges electrically connected to a high-voltage direct-current supply, from which the liquid emerges, forming cusps and jets when the voltage supply and liquid flow rates are suitably adjusted according to the type of liquid being sprayed. For a given jet (and thus droplet) size, and a given liquid, this nozzle may enable a higher flow rate to be achieved than those in which a single cusp
35 and jet are used.

Figure 5, shows one example of an array of six nozzles (1) in a circular pattern, centrally mixing the sprays.

Liquid Supply Means

An example of such a device is illustrated in Fig. 6 which shows an ion stream method, wherein a high voltage electrode (5) breaks up pairs of charge carriers within the liquid, thus neutralizing those of opposite polarity at the electrode, and leaving a large population of monionized like-polarity charge carriers which stream away from the high voltage electrode by coulombic force, thus moving the liquid in the direction of the counter electrode (6) by means of viscous drag. This pumping means requires that an electrode (5) is able to effectively inject like-polarity charge carriers into the liquid, close to the electrode (5). This may be effectively done by using a sharp-edged conducting or semiconducting surface, held at a sufficiently high potential to disrupt lightly bonded charge carriers or to ionize the liquid. Normally, it is only possible to establish a strong enough field for both creating unipolar charge carriers and pumping the liquid, when the liquid is of sufficient resistivity. Typically a resistivity of, say 10 (exp. 8) ohm meters, will pump at several millilitre per minute, with a head of up to one meter, at a voltage of 10 to 20 kilovolts, and a direct current of only a few microamperes. More conductive liquids will draw more current and will establish a weaker electric field. Thus highly conducting liquids, such as, say tap water may not establish a practicable drag pressure.

Figure 7 shows an example of the novel pump of the invention in which a plastic tube (7a), 1.0cm long, internal diameter 1.0 cm and 0.8 mm wall thickness has one of a pair of disc-shaped wire gauze electrodes (8a and 8b) bonded to each of its ends. A source of d.c. voltage is connected to each electrode. Liquid is supplied to and taken from tube (7a) by two further plastic tubes (7b and 7c) one of each being bonded to each wire gauze electrode (8a or 8b). Glass tube (7a) is filled with powdered silica (9). In operation, on applying a voltage to the electrodes (8a and 8b) a net forward force is exerted on the liquid which is interfaced with the silica (9) due to the presence of a double layer of charge at the solid-liquid interface. The polarity of the dc voltage is set so as to draw the liquid in the required direction, according to the polarity of the charge layer residing in the liquid at the liquid-solid interface. The pressure developed may be enhanced by using a solid of finer mesh size, thereby increasing n (see Scheme(I) above), with a maximized specific surface and with maximal zeta potential difference at the solid-liquid interface. Electrode voltages may be adjusted in accordance with the length of the current path between the two electrodes, so as to limit current flow to a desired value.

Using the device illustrated in Figure 6 a flow rate of 0.03 mL sec^{-1} was obtained with mineral oil of resistivity 10^7 ohm m , relative permittivity ~ 2.5 and viscosity 22 centistokes with an applied voltage of 20kV.

Electrical Charging Means

An example of this is a piezo electric generator. Figure 8 illustrates a pair of piezoelectric ceramic generators (10) (11) which may be easily squeezed by a cam

(12) operated by a trigger-shaped lever (13). The entire assembly may be housed in a strong steel frame, (14), and the piezoelectric pair may be held tight by adjustment screw (15). The voltage terminals (16) are the two live electrodes for connection to the pumps and nozzles, whilst terminal (17) is earthed, say to the steel frame.

5 When the lever (13) is pulled inward, the two ceramic generators (10) and (11) will produce high voltages upon the terminals (16) placed at the end surfaces, which may be used to activate both the electrokinetic pumps and the nozzles.

10 Typical values of charge from say a barium titanate ceramic of about 1.0cm length and 1.0 sq cm surface area would be 1.0 or 2.0 microcoulomb per squeeze, of either positive or negative polarity. Upon release of the squeezing pressure, a similar charge will flow in the opposite direction. A typical voltage would be say 5,000 to 10,000 volts. Thus, pumping and atomizing may both be achieved by hand operation of a single pair of piezoelectric generators at appropriate voltages, say 5,000 volts, and sufficient currents, say 2.0 microcoulombs per second (2.0 microamperes).

15 The piezoelectric material may be chosen from several types, such as barium titanate ceramic, or pvdf polymers, which generate significant high-voltage electric charge displacement upon being pressurized. The choice and capacity may be so chosen as to offer control of the degree of pumping and/or atomization when operated. The liquid flow induction, and the nozzle atomization will occur when the
20 piezo-electric generators are squeezed, and again (with opposite polarity) when the piezo-electric generators are released from pressure. The device is arranged so that when squeezed, and when released, the pumps and nozzles will operate without alteration of flow rate or droplet size. Only polarity will change (reverse) in the two modes of operation arising from pressure and release of pressure. This will maintain
25 constant flow and droplet generation, and mixing of species and/or charge-to-mass ratio adjustment of the sprays, during the active modes of pressure, and release of pressure.

Particular examples of the dispenser of the invention are illustrated below:

30 Figure 9 shows a dispenser of the invention, in which liquid in each of two reservoirs (20) is caused to flow along suitable conduit, say polyethelene tubing (21) into two electrokinetic pumps (22), say by gravity feed. The two piezoelectric generators (23) are then squeezed so that a high voltage charge is induced at the two faces of the piezoelectric materials. These high voltages will then appear at the terminals of the pumps (22), which are electrically connected to the piezoelectric
35 material by wire conductors.

At the same time, these high voltages will appear at the two conducting, or semi-conducting, capillary-tube nozzles (24). Thus, when the two liquids reach the two nozzles, the liquids will emerge from the nozzles as comminuted droplets with

electrical charges of opposing polarity. The droplets will then be attracted to each other by electric field forces, and will tend to mix vigorously.

The value of droplet charge on each of the two streams of droplets may be independently adjusted to produce the optimum residual value by one or more of several means: the size, shape, and/or materials of the two piezoelectric materials may be set to give differing values of voltage and charge; the two liquid flow rates may also be adjusted, either by suitable design of the two electrokinetic pumps, or by differing values of piezoelectric voltage applied to the two pumps thus directly influencing droplet charge for a given voltage and nozzle design; and the droplet size and charge of the two liquids may be independently adjusted by the formulations of the two liquids, especially by adjustment of the liquid resistivities.

A second example of the dispenser of the invention is illustrated in Figure 10: Two identical syringes (30a and 30b) are actuated by a rigid plate (31), the plate being attached to a motor drive unit. Two identical capillary nozzles (32a and 32b) each with internal diameters of 0.5mm are each interconnected with one of the syringes (30a or 30b) by one of a pair of flexible tubes (33a and 33b). Each nozzle (32a and 32b) is fixed in a non-conducting mounting (34a or 34b respectively) so as to define an angle of approximately 90° with each other. One nozzle (32a) is attached to a high voltage source (35a) of (+) 6.7 kilovolts and the other nozzle (32b) is attached to a high voltage source (35b) of (-) 6.7 kilovolts.

In one particular experiment using the above described device, the flow rates of liquid (a mixture of 80% ethanol and 20% polyethylene glycol) from each syringe was adjusted to 1.0µL/sec. The nozzles were attached to the high voltage sources of (+) and (-) 6.7 kVolts respectively. The two spray clouds were observed to mix virtually completely to provide an electrically neutral spray.

Claims

1. A device for comminuting a liquid, which comprises at least two electrohydrodynamic comminution means arranged so that in use comminutions of opposing polarity are formed which are substantially admixed after formation.
2. A device according to claim 1, wherein each comminution means comprises a comminution site, a means for supplying a liquid to the comminution site and a means for electrically charging the comminution site to an electric potential sufficient to comminute the liquid in use.
3. A device according to claim 1 or claim 2, which comprises 2, 4 or 6 comminution means.
4. A device for comminuting a liquid, which comprises at least two electrohydrodynamic comminution means each comprising a comminution site, a means for supplying a liquid to the comminution site and a means for electrically charging the comminution site to an electric potential sufficient to comminute the liquid in use, wherein the comminution means are arranged so that in use comminutions of opposing polarity are formed which are then substantially admixed.
5. A device according to claim 6, wherein the generator is a piezoelectric generator.
6. A device according to any one of claims 1 to 5, which comprises a means for regulating the electrical charge on a comminution formed from any of the comminution means prior to admixture.
7. A device according to claim 6, wherein the means for regulating the electrical charge on a comminution comprises a means for regulating the charging means so as to provide variable voltage output and/or a means for regulating the means for supplying a liquid to the comminution site so as to vary the liquid flow rate to the comminution site.
8. A device according to any one of claims 1 to 7, wherein the comminution means are arranged so that the comminutions produced are directed to converge into a mixing zone.

9. A device according to claim 8, which comprises two comminution means angled towards each other so as to produce comminutions which converge into the mixing zone.
- 5 10. A device according to claim 8, which comprises three or more comminution means arranged so that the comminutions are directed to converge radially into the mixing zone.
11. A device according to claim 8, wherein the comminution means are located in
10 a mutually parallel manner such that the mutual attraction of the comminutions produced is sufficient to allow substantial admixing.
12. A device according to any one of claims 8 to 11, wherein one liquid supply means supplies all of the comminution means.
- 15 13. A device according to any one of claims 1 to 12, adapted for the dispensation of a comminuted liquid for inhalation.
14. A device for comminuting a liquid for inhalation, which comprises at least
20 two electrohydrodynamic comminution means each comprising a comminution site, a means for supplying a liquid to the comminution site and a means for charging the comminution site to an electric potential sufficient to comminute the liquid in use, wherein the comminution means are arranged so that in use comminutions of opposing polarity are formed which are substantially admixed after formation.
- 25 15. A device according to claim 14, adapted for dispensing perfumes and aromas.
16. A device according to any one of claims 1 to 15, in the form of an inhaler, for
the inhaled delivery of a medicament.
- 30 17. A pump for pumping liquid, which comprises an electrically insulating conduit for the liquid, the conduit enclosing an electrically insulating solid permeable to liquid, means for retaining the solid within the conduit and means for applying an electric field across the solid, so that in use, when the electric field is applied, liquid is
35 induced to flow through the solid and hence along the conduit.
18. A pump according to claim 17, wherein the means for applying an electric field across the solid is a pair of permeable electrodes, spaced apart along the conduit.

19. A pump according to claim 17 or 18, wherein the means for applying an electric field across the solid also acts as the retaining means for the solid in the conduit.
- 5 20. A pump according to any one of claims 17 to 19, wherein each of the pair of permeable electrodes are fixed apart along the conduit and the permeable solid substantially fills the space defined by the electrodes and the inner wall or walls of the conduit.
- 10 21. A pump according to any one of claims 17 to 20, wherein the electrically insulating solid is in powdered form.
22. A pump according to claim 21, which comprises an electrically insulating tube, a pair of electrodes permeable to liquid and fixed apart along the tube and a
15 powdered solid permeable to liquid, the solid substantially filling the space defined by the electrodes and the inner wall of the tube and means for applying an electric field to the electrodes, so that in use, when the field is applied, liquid is induced to flow through the solid and hence along the tube.

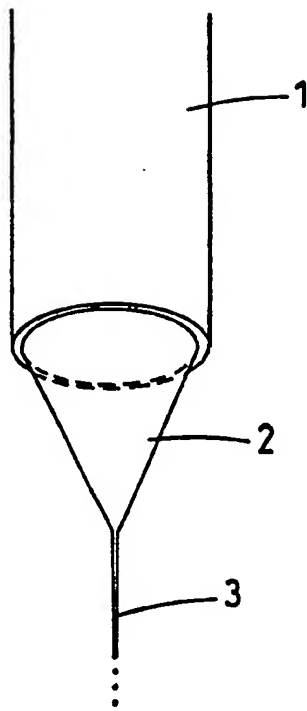


Fig. 1

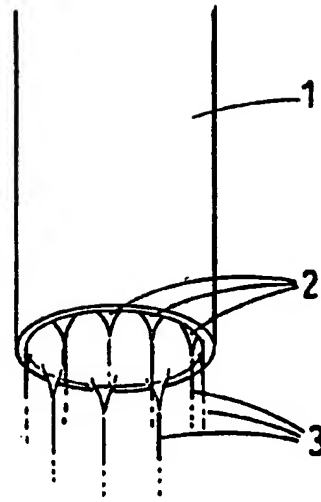


Fig. 2

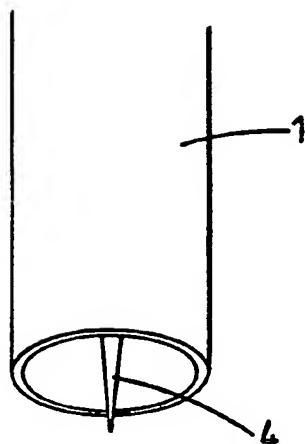


Fig. 3

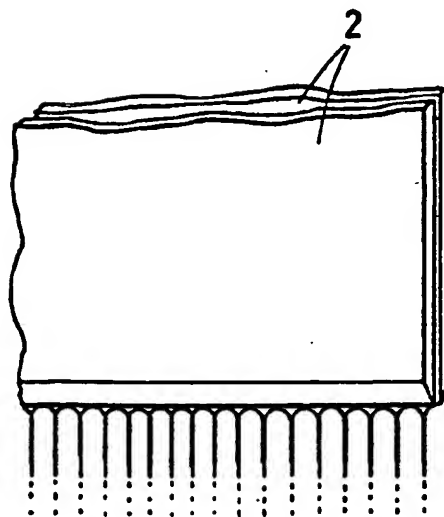


Fig. 4

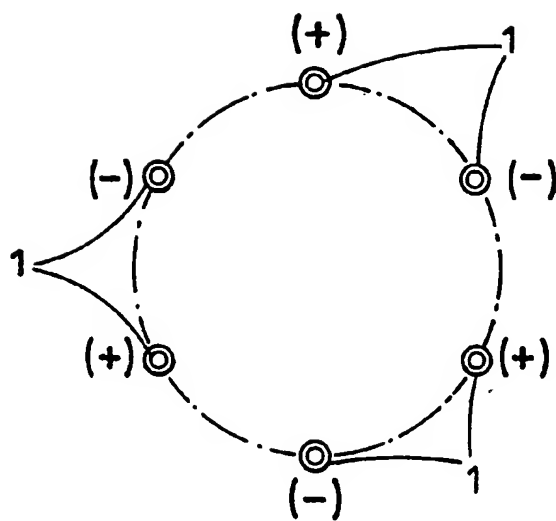


Fig. 5

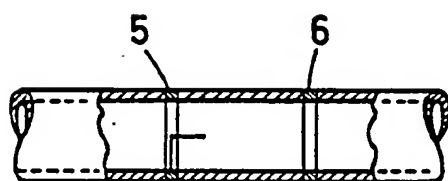


Fig. 6

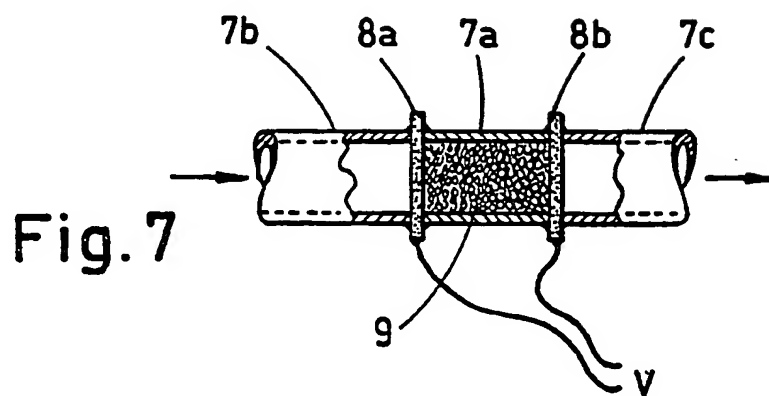


Fig. 7

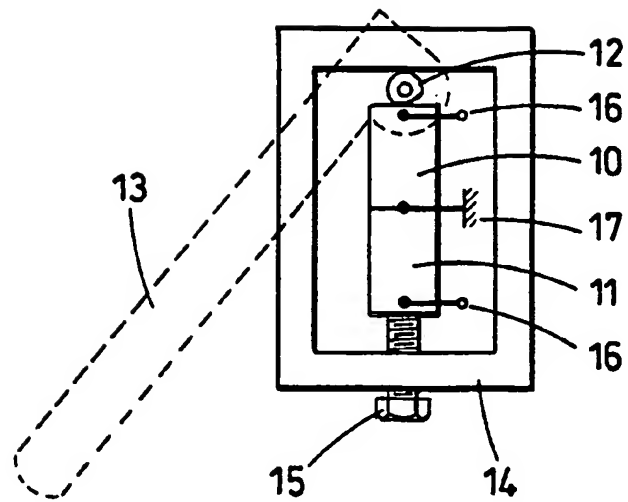


Fig. 8

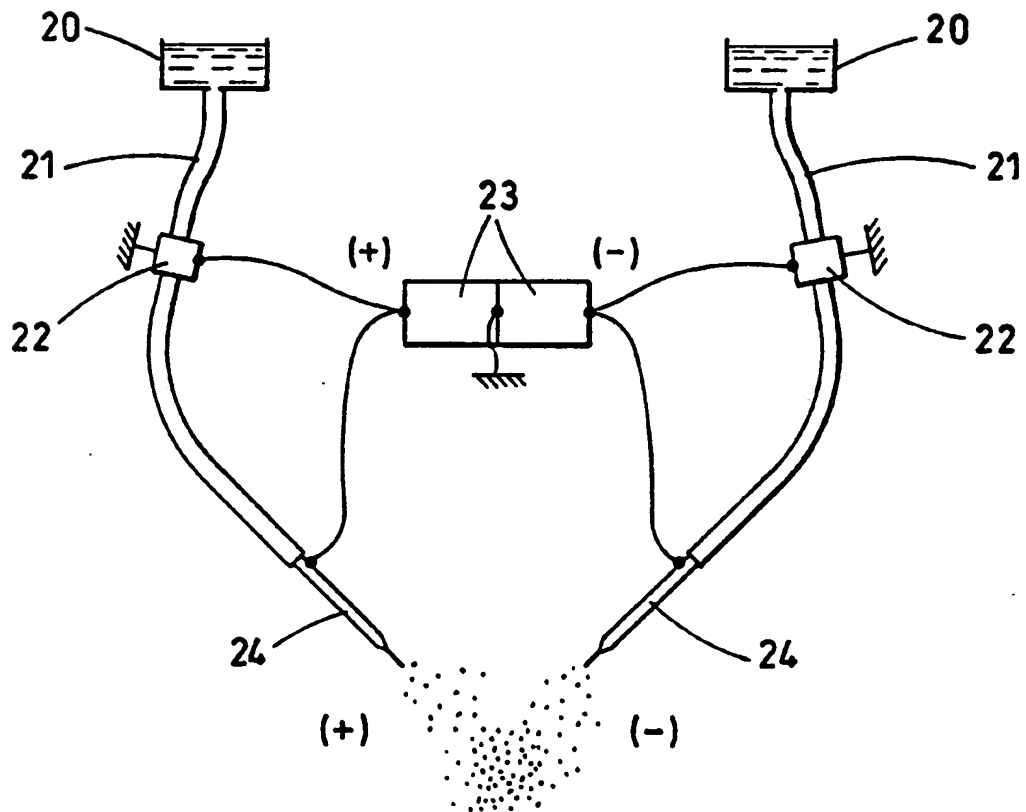


Fig. 9

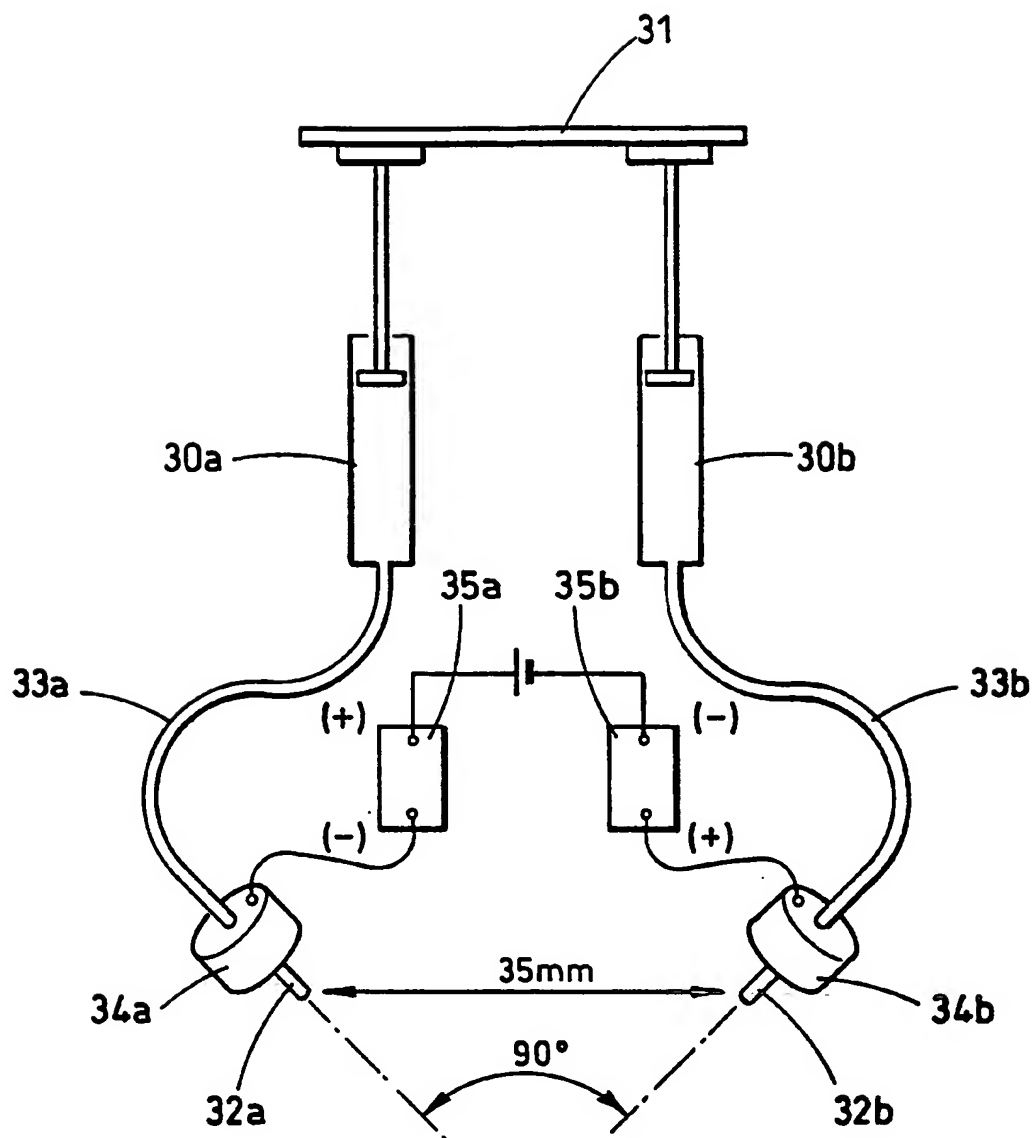


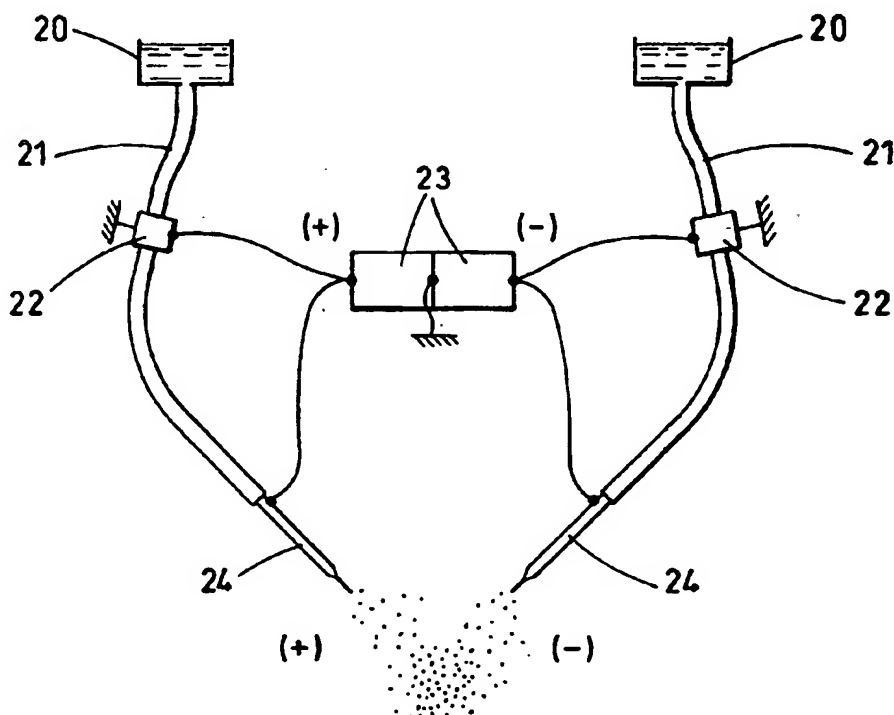
Fig.10



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : B05B 5/025, 5/053, 5/16	A3	(11) International Publication Number: WO 94/12285 (43) International Publication Date: 9 June 1994 (09.06.94)
<p>(21) International Application Number: PCT/GB93/02443</p> <p>(22) International Filing Date: 26 November 1993 (26.11.93)</p> <p>(30) Priority Data: 9225098.4 1 December 1992 (01.12.92) GB</p> <p>(71) Applicant (for all designated States except US): ELECTROSOLS LTD. [GB/GB]; Thursley Copse, Farnham Lane, Haslemere, Surrey GU27 1HA (GB).</p> <p>(72) Inventor; and (75) Inventor/Applicant (for US only): COFFEE, Ronald, Alan [GB/GB]; Thursley Copse, Farnham Lane, Haslemere, Surrey GU27 1HA (GB).</p> <p>(74) Agent: RUTTER, Keith; SmithKline Beecham, Corporate Intellectual Property, Great Burgh, Yew Tree Bottom Road, Epsom, Surrey KT18 5XQ (GB).</p>	<p>(81) Designated States: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 13 October 1994 (13.10.94)</p>	

(54) Title: DISPENSING DEVICE



(57) Abstract

A device for comminuting a liquid, which comprises at least two electrohydrodynamic comminution means (24) arranged so that in use comminution of opposing polarity are formed which are substantially admixed after formation and a pump (22) for use in the dispensing device.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 93/02443

A. CLASSIFICATION OF SUBJECT MATTER

IPC 5 B05B5/025 B05B5/053 B05B5/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 5 B05B F04B F04D H02N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US,A,4 508 265 (JIDO) 2 April 1985 see column 3, line 45 - column 4, line 11; figures	1-4,6-9
Y	---	13-16
X	FR,A,2 266 584 (RANSBURG CORPORATION) 31 October 1975 see page 8, line 18 - line 30; figures	1-4,8-10
Y	---	13-16
Y	EP,A,0 234 842 (IMPERIAL CHEMICAL INDUSTRIES PLC) 2 September 1987 see abstract; figures	13-16
A	---	5
	GB,A,2 128 900 (THEOKTISTE CHRISTOFIDIS) 10 May 1984 see abstract; figure	

	---/---	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Date of the actual completion of the international search

3 August 1994

Date of mailing of the international search report

23.08.94

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 93/02443

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PATENT ABSTRACTS OF JAPAN vol. 1, no. 157 (C-032) 14 December 1977 & JP,A,52 098 040 (SHIMIZU KOICHI) 17 August 1977 see abstract ---	1,4
X	PRODUCT ENGINEERING, no.14, 6 July 1970 pages 71 - 72 RAY LEWIS 'Electro-osmosis controls fluid in novel transducer concept' see the whole document ---	17,18, 20-22
X	DE,A,27 20 523 (NISSAN MOTOR CO, LTD.) 24 November 1977 see page 21, paragraph 3 - page 22, paragraph 3; figures 12-15 ---	17,18
X	WO,A,91 02375 (FRAUNHOFER-GESELLSCHAFT ZUR FÖRDERUNG DER ANGEWANDTEN FORSCHUNG E.V.) 21 February 1991 see page 1 see page 8, paragraph 2; figure 5 ---	17,18
A	EP,A,0 102 713 (IMPERIAL CHEMICAL INDUSTRIES PLC) 14 March 1984 see abstract; figures ---	17
A	US,A,2 945 443 (PETER L. AUER ET AL.) 19 July 1960 see column 1, line 58 - column 2, line 19; figure 1 -----	17

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB93/02443

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

The claims of the present application contain two different subject-matters:

a - Claims 1-16: a device for comminuting a liquid which comprises at least two electrohydrodynamic comminution means arranged so that in use comminutions of opposing polarity are formed which are then substantially admixed.

b - Claims 17-22: a pump for pumping liquid comprising an electrically insulating solid permeable to liquid and means for applying an electric field across the solid, so that in use, when the electric field is applied, liquid is induced to flow through the solid.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 93/02443

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-4508265	02-04-85	JP-C- 1327513 JP-A- 57209664 JP-B- 60057907	30-07-86 23-12-82 17-12-85
FR-A-2266584	31-10-75	US-A- 3930061 AU-A- 7921775 CA-A- 1051285 DE-A, C 2514371 GB-A- 1507341 JP-C- 1392561 JP-A- 50138038 JP-B- 61054464	30-12-75 23-09-76 27-03-79 09-10-75 12-04-78 23-07-87 04-11-75 22-11-86
EP-A-0234842	02-09-87	AU-B- 582949 AU-A- 6906187 AU-B- 594429 AU-A- 6906287 CA-A- 1275883 EP-A- 0234841 JP-A- 62197071 JP-A- 62254830 US-A- 4829996 US-A- 4795330	13-04-89 27-08-87 08-03-90 27-08-87 06-11-90 02-09-87 31-08-87 06-11-87 16-05-89 03-01-89
GB-A-2128900	10-05-84	NONE	
DE-A-2720523	24-11-77	JP-A- 52135988 JP-A- 53000390 JP-A- 53001324 CA-A- 1109545 GB-A- 1571201 US-A- 4203398	14-11-77 05-01-78 09-01-78 22-09-81 09-07-80 20-05-80
WO-A-9102375	21-02-91	DE-C- 3925749 EP-A, B 0469019 JP-T- 5501026 US-A- 5180288	31-10-90 05-02-92 25-02-93 19-01-93
EP-A-0102713	14-03-84	AU-B- 574327 AU-A- 1720783	07-07-88 01-03-84

INTERNATIONAL SEARCH REPORT

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International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0102713		CA-A- 1200687	18-02-86
		GB-A, B 2126431	21-03-84
		JP-A- 59062359	09-04-84
		SU-A- 1279547	23-12-86
		US-A- 4634057	06-01-87
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US-A-2945443		NONE	
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